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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

**In re United States Patent Application of:**

**Appellant: Jason C.H. SHIH**

**Serial No.: 10/007,613**

**Date Filed: October 26, 2001**

**Title: METHOD AND COMPOSITION  
FOR STERILIZING SURGICAL  
INSTRUMENTS**

**Docket No.: 4171-102 CIP**

**Examiner: Zachariah LUCAS**

**Art Group: 1648**

**Confirm. No.: 4213**

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**23448**

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*Candace White*

Candace White

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**BRIEF ON APPEAL**

Mail Stop Appeal Brief – Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This is an appeal under 35 U.S.C. §134 from the Final Rejection in the Office Action dated June 30, 2004 Office Action, of claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 of U.S. Patent Application No. 10/007,613.

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### **REAL PARTY IN INTEREST**

The real party in interest in this appeal is BioResource International, Inc., the owner of the invention and patent rights of this application, by virtue of an Assignment of U.S. Patent Application No. 10/007,613 recorded in the assignment records of the U.S. Patent and Trademark Office on October 26, 2001 at reel 012366, frame 0566 (3 pages).

### **RELATED APPEALS AND INTERFERENCES**

There are no other appeals or interferences known to Appellant, the Appellant's legal representative, or assignee, which will directly effect or be directly affected by or have a bearing on the Board's decision in this appeal.

### **STATUS OF CLAIMS**

A complete listing of claims 1-83 of the present application is attached in **Appendix A** hereof, among which claims 1-51, 53-56, 63, 68, 69, 71, 73, 74-80, and 82 are currently pending in the subject application.

Process claims 1-38 have been withdrawn from consideration in response to the restriction requirement imposed by the Examiner in the September 9, 2003 Office Action. Appellant intends to rejoin the withdrawn process claims 1-38 under MPEP §821.04 at a later time when the elected product claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are determined to be allowable.

Claims 68, 69, and 75-79 have been withdrawn from consideration as being directed to non-elected species of proteolytic enzymes. Since claim 39 is a generic claim that covers both elected and non-elected enzyme species, claims 68, 69, and 75-79 will be entitled to consideration upon allowance of such generic claim 39.

Remaining claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 have been finally rejected under 35 U.S.C. §103(a) by the Examiner in the June 30, 2004 Office Action, and such rejected claims are the subject of this appeal.

### **STATUS OF AMENDMENTS**

In the August 30, 2004 Response to Office Action, Appellant cancelled claims 52, 57-61, and 64-65, and amended claims 39, 51, 53-56, 71, 80, and 82.

Such cancellation and amendments of claims were subsequently approved by the Examiner and entered for purpose of appeal in the September 22, 2004 Advisory Action.<sup>1</sup>

With the timely submission of a Notice of Appeal and this Appeal Brief with the required fees, the Response filed August 30, 2004 has perfected the record of the instant application on appeal, and the rejected claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 as amended in such Response are the subject of this appeal to the Board.

### **SUMMARY OF THE INVENTION**

The claimed invention of the present application broadly relates to systems and methods for disinfecting and sterilizing medical devices and like articles that are susceptible to contamination by infectious prion proteins, by **combining thermal treatment and enzymatic degradation**.

Specifically, the treated articles are heated to an elevated temperature and exposed to a proteolytic enzyme, either successively at two different durations or simultaneously.

The thermal treatment functions to render the infective prion protein proteolytically susceptible. The temperature for conducting such thermal treatment is below the pyrolytic destruction temperature of the infective prion protein, and preferably at least 40°C but not more than 150°C.

The enzymatic degradation uses a thermally stable proteolytic enzyme, such as keratinase or subtilisin, for reducing or degrading the infective prion protein, which has been rendered proteolytically susceptible by the thermal treatment. The temperature for conducting such enzymatic degradation is preferably from about 50°C to about 65°C.

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<sup>1</sup> The September 22, 2004 Advisory Action contains several self-evident typographic error: (a) Claim(s) rejected should be 39-51, 53-56, 63, 71, 73, 74, 80 and 82, instead of "35-51, 53-56, 63, 71, 73, 74, 80 and 82" as listed in Section (7) of the September 22, 2004 Advisory Action; (b) Claim(s) withdrawn from consideration should be 1-38, 68, 69 and 75-79, instead of "68, 69 and 75-79" as listed in Section (7) of the September 22, 2004 Advisory Action.

The specific features of the pending claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are set out below in tabular format, cross-referenced to disclosure in the specification by page and line number, to facilitate the Board's review:

| Claim No. | Features Recited by the Claim  | Cross-Reference to the Specification  |
|-----------|--|---|
| Claim 39  | <p>"A system comprising:</p> <p>(a) one or more articles susceptible to contamination by infectious prion protein;</p> <p>(b) means for heating said articles;</p> <p>(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and</p> <p>(d) means for exposing said articles to said proteolytic enzyme,</p> <p>wherein said one or more articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration."</p> | <p>Page 4, lines 15-21; page 5, lines 1-19.</p> <p>Page 6, lines 8-21.</p> <p>Page 10, line 21; page 11, lines 1-2.</p> <p>Page 6, lines 3 and 6.</p> |
| Claim 40  | "wherein the proteolytic enzyme comprises keratinase."   | Page 6, line 14.  |
| Claim 41  | "wherein the keratinase is provided in a solution at a concentration within a range of from about 0.2 g/L to about 1.0 g/L."   | Page 7, lines 3-5.  |
| Claim 42  | "wherein the solution comprises a solvent selected from the group consisting of distilled water, alcohol, buffer solution, and detergent solution."  | Page 8, lines 11-13.  |
| Claim 43  | "wherein said solution further comprises one or more chemical additives selected from the group consisting of surfactants, builders, boosters, and fillers."   | Page 8, lines 14-17.  |
| Claim 44  | "wherein said articles comprise surgical instruments."   | Page 5, lines 1-2.  |
| Claim 45  | "wherein said surgical instrument(s) are selected from the group consisting of: clamps, forceps, scissors, knives, cables, punches, tweezers, cannulae, calipers, carvers, curettes, scalers, dilators, clip applicators, retractors, contractors, excavators, needle holders, suction tubes, trocars, coagulation electrodes, electroencephalographic depth electrodes, rib and   | Page 5, lines 2-5.  |

| Claim No. | Features Recited by the Claim  | Cross-Reference to the Specification   |
|-----------|--|--|
|           | sternum spreaders, bipolar probes, and rib shears.”  |  |
| Claim 46  | “wherein said articles comprise cutleries and kitchen utensils.”   | Page 5, lines 7-8.   |
| Claim 47  | “wherein said cutleries and kitchen utensils are selected from the group consisting of: knives, forks, scissors, peelers, parers, slicers, spatulas, and cleavers.”  | Page 5, line 9.  |
| Claim 48  | “wherein said laboratory apparatuses are selected from the group consisting of: containers, filtration devices, centrifuges, spectrophotometers, and fluorometers.”  | Page 5, lines 14-19.   |
| Claim 49  | “wherein said article(s) comprise veterinary devices.”   | Page 5, line 12.   |
| Claim 50  | “wherein said veterinary devices are selected from the group consisting of clamps, forceps, knives, saws, probes, and electronic stun equipment.”  | Page 5, lines 12-13.   |
| Claim 51  | “wherein said first elevated temperature is higher than said second elevated temperature.”   | Page 6, lines 3-4.   |
| Claim 53  | “wherein said first elevated temperature is at least about 60°C.”  | Page 11, lines 1-2.  |
| Claim 54  | “wherein said first elevated temperature is in a range of from about 100°C to about 150°C.”  | Page 11, line 3.   |
| Claim 55  | “wherein said first elevated temperature is at least about 75°C.”  | Page 11, line 2.   |
| Claim 56  | <p>“A system comprising:</p> <p>(a) one or more articles susceptible to contamination by infectious prion protein;</p> <p>(b) means for heating said one or more articles;</p> <p>(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and</p> <p>(d) means for exposing said articles to said proteolytic enzyme;</p> <p>wherein said one or more articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to said proteolytic enzyme.”</p> | <p>Page 4, lines 15-21; page 5, lines 1-19; page 11, lines 5-16.</p> <p>Page 6, lines 8-21.</p> <p>Page 15, lines 16-17.</p> |
| Claim 63  | “wherein the proteolytic enzyme comprises a keratinase enzyme.”  | Page 6, line 14.   |

| Claim No. | Features Recited by the Claim   | Cross-Reference to the Specification  |
|-----------|---|---|
| Claim 71  | <p>“A system comprising (a) a surgical instrument contaminated with infective prion protein; (b) means for heating the surgical instrument; (c) a proteolytic enzyme that is thermally stable at a temperature in a range of from about 35°C to about 100°C and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument, and (d) means for exposing the surgical instrument to the proteolytic enzyme, wherein said surgical instrument is characterized by a first elevated temperature in a range of from about 100°C to about 150°C during a first duration, and wherein said surgical instrument is characterized by a second elevated temperature in a range of from about 35°C to about 100°C and exposure to said proteolytic enzyme during a second, subsequent duration.”</p> | <p>Page 4, lines 15-21.</p> <p>Page 6, line 4; page 12, lines 10-12.</p> <p>Page 11, line 3.</p> <p>Page 6, line 4.</p>                               |
| Claim 73  | <p>“wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins, chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidase, thermolysins, bacillolysin, mycylisins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.”</p>   | <p>Page 12, lines 18-21; page 13, lines 1-2.</p>  |
| Claim 74  | <p>“wherein the proteolytic enzyme comprises <i>Bacillus licheniformis</i> PWD-1 keratinase.”</p>   | <p>Page 13, lines 3-4.</p>  |
| Claim 80  | <p>“A system comprising:</p> <p>(a) one or more articles susceptible to contamination by infectious prion protein;</p> <p>(b) means for heating said articles;</p> <p>(c) <i>Bacillus licheniformis</i> PWD-1 keratinase; and</p> <p>(d) means for exposing the heated articles to the <i>Bacillus licheniformis</i> PWD-1 keratinase,</p> <p>wherein said articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, and wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the <i>Bacillus licheniformis</i> PWD-1 keratinase during a second, subsequent duration.”</p>  | <p>Page 4, lines 15-21; page 5, lines 1-19.</p> <p>Page 13, lines 3-4.</p> <p>Page 10, line 21; page 11, lines 1-2.</p> <p>Page 6, lines 3 and 6.</p> |
| Claim 82  | <p>“A system comprising:</p> <p>(a) one or more articles susceptible to</p>   | <p>Page 4, lines 15-21; page 5, lines 1-19; page 11, lines 5-16</p>   |

| Claim No. | Features Recited by the Claim   | Cross-Reference to the Specification             |
|-----------|---|--|
|           | contamination by infectious prion protein;<br>(b) means for heating said articles;<br>(c) <i>Bacillus licheniformis</i> PWD-1 keratinase; and<br>(d) means for exposing the articles to <i>Bacillus licheniformis</i> PWD-1 keratinase,<br>wherein said articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to the <i>Bacillus licheniformis</i> PWD-1 keratinase.” | Page 13, lines 3-4.<br><br>Page 15, lines 16-17. |

### REFERENCES

The following references were cited under 35 U.S.C. §103(a) in the June 30, 2004 Office Action finally rejecting the pending claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82:

- (a) WHO Infection Control Guidelines for Transmissible Spongiform Encephalopathies: Report of a WHO Consultation, WORLD HEALTH ORGANIZATION (WHO), March 23-26, 1999 (hereinafter “WHO Document”);
- (b) **Huth** et al. U.S. Patent No. 6,448,062 (hereinafter “Huth”);
- (c) **Vlass** et al. U.S. Patent No. 6,210,639 (hereinafter “Vlass”);
- (d) **Potgeiter** et al. U.S. Statutory Invention Registration No. H1,818 (hereinafter “Potgeiter”);
- (e) **Shih** U.S. Patent No. 5,171,682 (hereinafter “Shih”);
- (f) **Bolton** et al., Molecular Characteristics of the Major Scrapie Prion Protein (hereinafter “Bolton”); and
- (g) **Oesch** et al. Properties of the Scrapie Prion Protein: Quantitative Analysis of Protease Resistance (hereinafter “Oesch”).

### ISSUES

In the September 22, 2004 Advisory Action, the Examiner has withdrawn various previously-raised claim rejections, including the rejections for lack of enablement and new matter.

The only two remaining issues are:

- (1) Whether it is appropriate for claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 to recite systems that include articles susceptible to contamination by infectious prion protein.

- (2) Whether claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are unpatentable under 35 U.S.C. §103(a) as being obvious over the WHO Document as the primary reference, in view of numerous secondary references including **Huth, Vlass, Potgeiter, Shih, Bolton, and Oesch.**

### **GROUPING OF THE CLAIMS**

Group I: Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 constitute a unitary group of claims presenting common issues in respect of their patentability. Claim 39 is representative of the group.

### **ARGUMENT**

#### **Issue 1 - Propriety of Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 in Reciting Systems that Include Articles Susceptible to Contamination by Infectious Prion Protein – Claim 39 is Representative**

In the June 30, 2004 Office Action, the Examiner objected to claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82, on the ground that such claims are directed to systems for treating articles that may be infected with prion proteins, and that it is inappropriate for such claims to include the articles to be treated in the claimed systems for treating the articles.

In response to such objection, the Appellant has amended claims 39 (from which claims 40-51, 53-55, and 63 depend), 56, 71 (from which claims 73 and 74 depend), 80 and 82 in the August 30, 2004 Response to recite simply **a system**, which **comprises** one or more articles susceptible to contamination by infectious prion protein, means for heating such articles, a proteolytic enzyme, and means for exposing such articles to the proteolytic enzyme (see claims 39, 56, 71, 80, and 82 as amended).

As a result of such amendments, claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 are no longer limited to systems or apparatuses for treating prion-contaminated articles. Instead, they are now directed to **a system that includes both the contaminated articles and means for treating such articles**, and therefore overcome the Examiner's objections.

The Examiner's assertion in the September 22, 2004 Advisory Action that such amended claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 still read on system for the treatment of articles that may be infected by

prion proteins (see Advisory Action, page 2, second paragraph) is inconsistent with the claim language as amended in the August 30, 2004 Response and is incorrect.

Appellant therefore respectfully requests that the Board reverse the Examiner's objection to claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82.

**Issue 2 - Patentability of Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 under 35 U.S.C. §103(a) over the WHO Document in view of Huth, Vlass, Potgeiter, Shih, Bolton, and/or Oesch – Claim 39 is Representative**

This rejection is traversed because the Examiner failed to establish a *prima facie* case of obviousness to support such rejection.

The Office has the initial burden of showing a *prima facie* case of obviousness. *In re Bell*, 26 U.S.P.Q.2d 1529, 1530 (Fed. Cir. 1993). In order to properly establish a *prima facie* case of obviousness based on combination of several references, the Examiner must show a reason, suggestion, or motivation to lead an inventor to combine those references. *Pro-Mold and Tool Co. V. Great Lakes Plastics Inc.*, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

The representative claim 39 expressly requires:

“A system comprising:

- (a) one or more articles susceptible to contamination by infectious prion protein;
- (b) means for heating said articles;
- (c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins;  
and
- (d) means for exposing said articles to said proteolytic enzyme,

wherein said one or more articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration.”

The language of claim 39 expressly requires that the prion-contaminated articles be “characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration.”

Such express requirement in claim 39 further imposes **an implicit structural limitation**. Such system must provide **a specific arrangement of the recited elements, i.e., the articles, the heating means, the proteolytic enzyme, and the exposing means, to enable simultaneous heating and enzymatic digestion** of the prion-contaminated articles, so that the articles can be **characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration**, as required by claim 39.

**The cited references, either taken singularly or in combination, do not provide any derivative basis for such specific arrangement of articles, heating means, proteolytic enzyme, and exposing means, to allow the prion-contaminated articles to be characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration**, as expressly required by claim 39.

The primary reference cited by the Examiner, i.e., the WHO document, discloses sterilization of prion-contaminated surgical instruments by boiling or autoclaving with sodium hydroxide or sodium hypochlorite, followed by subsequent routine sterilization (see page 29, Appendix III, section 2 of the WHO document).

The Examiner conceded that the WHO Document does not teach usage of proteolytic enzyme for treating prion-contaminated articles, but attempted to remedy such deficiency of the WHO Document by combining teachings by various secondary references including Huth, Vlass, Potgeiter, Shih, Bolton, and/or Oesch about the use of proteolytic enzyme.

However, such hypothetical combination proposed by the Examiner only yields **a system containing a mere aggregate of** articles, heating means, proteolytic enzyme and exposing means, but **it does not provide any derivative basis for a specific arrangement of such elements** that enables simultaneous heating and enzyme exposure of the prion-contaminated articles in such manner that such articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the proteolytic enzyme during a second, subsequent duration, as expressly required by claim 39 of the present application. In fact, none of the secondary references acknowledges, or even recognizes, the advantages of arranging the articles, the heating means, the proteolytic enzyme and the exposing means for simultaneous heating and enzyme exposure to allow the articles to be at an elevated temperature in a range of from about 50°C to about 65°C during exposure to a proteolytic enzyme.

In the September 22, 2004 Advisory Action, the Examiner asserted that claim 39 of the present application does not structurally distinguish over the cited prior art references, on the basis that there are no teachings demonstrating that the system suggested by the combination of the cited prior art references would not be capable of performing the functions of simultaneous heating and enzyme exposure.

However, it is clear that a specific arrangement of articles, heating elements, proteolytic enzyme, and exposing means is necessary for a system to perform the functions of simultaneous heating and exposing the articles to the proteolytic enzyme.

**The system suggested by the combination of the cited prior art reference does not have such specific arrangement of articles, heating elements, proteolytic enzyme, and exposing means.**

Therefore, such prior art system is incapable of performing the functions of simultaneous heating and enzyme exposure.

Further, **it has been well-established that when the claimed invention contains functional limitations not suggested by the prior art reference, the mere fact that the prior art could be so modified to perform such functions would not have made the modification obvious, unless the prior art suggested the desirability of the modification.** See *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); see also *In re Mills*, 16 USPQ2d 1430 (CAFC 1990).

In this case, nothing in the cited references suggests the desirability of modifying the prior art system and re-arranging the prion-contaminated articles, the heating elements, the proteolytic enzyme, and the exposing means so as to allow simultaneous heating and enzyme exposure of the articles so that such articles are at elevated temperature in a range of from about 50°C to about 65°C during exposure to a proteolytic enzyme.

Therefore, claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 of the present application patentably distinguish over all cited references.

It therefore is respectfully requested that the Board take cognizance of the absence of any proper basis of the §103 rejection of claim 39, as representative of appealed claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82, and correspondingly reverse the Examiner's rejection of such claims.

## CONCLUSION

Based on the foregoing arguments and cited legal precedent, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the decision of the Examiner finally rejecting claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 now pending in the application, consistent with the patentability of such claims over the cited art references.

This brief is provided in triplicate. No oral hearing is requested.

Enclosed with this appeal brief is a Credit Card Payment form, authorizing the Office to charge the office fee in the amount of \$250.00 under 37 C.F.R. §1.17(c) to the credit card specified therein. Please charge any deficiency and credit any excess payment to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Respectfully submitted,



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## **APPENDIX A**

### **Appeal Claims 39-51, 53-56, 63, 71, 73, 74, 80, and 82 in a Listing of Claims 1-83**

1. (Withdrawn) A method of disinfecting article(s) that are susceptible to contamination by infectious prion protein, the method comprising the steps of:
  - (a) heating said article(s) to a sufficient temperature and for sufficient time to enhance the proteolytic susceptibility of infective prion protein associated with said article(s); and
  - (b) exposing the heated article(s) to a proteolytic enzyme that is effective for at least partial reduction of the infective protein prion associated with said article(s).
2. (Withdrawn) The method of claim 1, wherein said articles comprise surgical instruments.
3. (Withdrawn) The method of claim 2, wherein said surgical instrument(s) are selected from the group consisting of: clamps, forceps, scissors, knives, cables, punches, tweezers, cannulae, calipers, carvers, curettes, scalers, dilators, clip applicators, retractors, contractors, excavators, needle holders, suction tubes, trocars, coagulation electrodes, electroencephalographic depth electrodes, rib and sternum spreaders, bipolar probes, and rib shears.
4. (Withdrawn) The method of claim 1, wherein said article(s) comprise cutleries and kitchen utensils.
5. (Withdrawn) The method of claim 4, wherein said cutleries and kitchen utensils are selected from the group consisting of: knives, forks, scissors, peelers, parers, slicers, spatulas, and cleavers.
6. (Withdrawn) The method of claim 1, wherein said article(s) comprise laboratory apparatus(es).

7. (Withdrawn) The method of claim 6, wherein said laboratory apparatus(es) are selected from the group consisting of: containers, filtration devices, centrifuges, spectrophotometers, and fluorometers.
8. (Withdrawn) The method of claim 1, wherein said article(s) comprise veterinary devices.
9. (Withdrawn) The method of claim 8, wherein said veterinary devices are selected from the group consisting of clamps, forceps, knives, saws, probes, and electronic stun equipment.
10. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature not exceeding about 150°C.
11. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature of at least 35°C.
12. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature below about 150°C.
13. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature in a range of from about 100°C to about 150°C.
14. (Withdrawn) The method of claim 1, wherein the temperature in step (a) comprises a temperature in a range of from about 125°C to about 140°C.
15. (Withdrawn) The method of claim 1, wherein step (b) is conducted at lower temperature than step (a).
16. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature above about 40°C.

17. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature above about 50°C.
18. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 35°C to about 75°C.
19. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 40°C to about 75°C.
20. (Withdrawn) The method of claim 1, wherein step (b) is carried out at temperature in a range of from about 50°C to about 65°C.
21. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins, chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidase, thermolysins, bacillolysin, mycilysins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.
22. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a keratinase enzyme.
23. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises an active fragment of a keratinase enzyme.
24. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a *Bacillus licheniformis* PWD-1 enzyme or an active fragment thereof.

25. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a protease enzyme.
26. (Withdrawn) The method of claim 25, wherein the protease enzyme comprises a carbonyl hydrolase.
27. (Withdrawn) The method of claim 26, wherein the carbonyl hydrolase comprises subtilisin.
28. (Withdrawn) The method of claim 27, wherein the subtilisin comprises a mutant of wild-type *Bacillus amyloliquefaciens* subtilisin, comprising one or more amino acid substitutions, additions, or deletions.
29. (Withdrawn) The method of claim 25, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.
30. (Withdrawn) A method of removing infective prion protein from a surgical instrument contaminated with same, the method including (a) heating the surgical instrument at a temperature in a range of from about 100°C to about 150°C, followed by (b) exposing the heated surgical instrument to a proteolytic enzyme at a temperature in a range of from about 35°C to about 100°C at which the proteolytic enzyme is thermally stable and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument.
31. (Withdrawn) The method of claim 30, wherein said heating is conducted for a time of from about 5 minutes to about 5 hours.
32. (Withdrawn) The method of claim 30, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins,

chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidase, thermolysins, bacillolysin, mycylisins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.

33. (Withdrawn) The method of claim 30, wherein the proteolytic enzyme comprises *Bacillus licheniformis* PWD-1 keratinase.
34. (Withdrawn) The method of claim 1, wherein the proteolytic enzyme comprises a protease enzyme.
35. (Withdrawn) The method of claim 34, wherein the protease enzyme comprises a carbonyl hydrolase.
36. (Withdrawn) The method of claim 35, wherein the carbonyl hydrolase comprises subtilisin.
37. (Withdrawn) The method of claim 36 , wherein the subtilisin comprises a mutant of wild-type *Bacillus amyloliquefaciens* subtilisin, comprising one or more amino acid substitutions, additions, or deletions.
38. (Withdrawn) The method of claim 34, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.
39. (Previously presented) A system comprising:
  - (a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said articles;

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and

(d) means for exposing said articles to said proteolytic enzyme,

wherein said one or more articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to said proteolytic enzyme during a second, subsequent duration.

40. (Previously presented) The system of claim 39, wherein the proteolytic enzyme comprises keratinase.
41. (Previously presented) The system of claim 40, wherein the keratinase is provided in a solution at a concentration within a range of from about 0.2 g/L to about 1.0 g/L.
42. (Previously presented) The system of claim 41, wherein the solution comprises a solvent selected from the group consisting of distilled water, alcohol, buffer solution, and detergent solution.
43. (Previously presented) The system of claim 42, wherein said solution further comprises one or more chemical additives selected from the group consisting of surfactants, builders, boosters, and fillers.
44. (Previously presented) The system of claim 39, wherein said articles comprise surgical instruments.
45. (Previously presented) The system of claim 44, wherein said surgical instrument(s) are selected from the group consisting of: clamps, forceps, scissors, knives, cables, punches, tweezers, cannulae, calipers, carvers, curettes, scalers, dilators, clip applicators, retractors, contractors,

excavators, needle holders, suction tubes, trocars, coagulation electrodes, electroencephalographic depth electrodes, rib and sternum spreaders, bipolar probes, and rib shears.

46. (Previously presented) The system of claim 39, wherein said articles comprise cutleries and kitchen utensils.
47. (Previously presented) The system of claim 46, wherein said cutleries and kitchen utensils are selected from the group consisting of: knives, forks, scissors, peelers, parers, slicers, spatulas, and cleavers.
48. (Previously presented) The system of claim 47, wherein said laboratory apparatuses are selected from the group consisting of: containers, filtration devices, centrifuges, spectrophotometers, and fluorometers.
49. (Previously presented) The system of claim 39, wherein said article(s) comprise veterinary devices.
50. (Previously presented) The system of claim 49, wherein said veterinary devices are selected from the group consisting of clamps, forceps, knives, saws, probes, and electronic stun equipment.
51. (Previously presented) The system of claim 39, wherein said first elevated temperature is higher than said second elevated temperature.
52. (Cancelled).
53. (Previously presented) The system of claim 39, wherein said first elevated temperature is at least about 60°C.
54. (Previously presented) The system of claim 39, wherein said first elevated temperature is in a

range of from about 100°C to about 150°C.

55. (Previously presented) The system of claim 39, wherein said first elevated temperature is at least about 75°C.

56. (Previously presented) A system comprising:

(a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said one or more articles;

(c) a proteolytic enzyme selected from the group consisting of keratinases and subtilisins; and

(d) means for exposing said articles to said proteolytic enzyme;

wherein said one or more articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to said proteolytic enzyme.

57-61. (Cancelled).

63. (Previously presented) The system of claim 39, wherein the proteolytic enzyme comprises a keratinase enzyme.

64-67. (Cancelled).

68. (Withdrawn) The system of claim 39, wherein the proteolytic enzyme comprises subtilisin.

69. (Withdrawn) The system of claim 68, wherein the subtilisin comprises a mutant of wild-type *Bacillus amyloliquefaciens* subtilisin, comprising one or more amino acid substitutions, additions, or deletions.

70. (Cancelled).

71. (Previously presented) A system comprising (a) a surgical instrument contaminated with infective prior protein; (b) means for heating the surgical instrument; (c) a proteolytic enzyme that is thermally stable at a temperature in a range of from about 35°C to about 100°C and proteolytically effective to at least partially destroy the infective prion protein contaminating said surgical instrument, and (d) means for exposing the surgical instrument to the proteolytic enzyme, wherein said surgical instrument is characterized by a first elevated temperature in a range of from about 100°C to about 150°C during a first duration, and wherein said surgical instrument is characterized by a second elevated temperature in a range of from about 35°C to about 100°C and exposure to said proteolytic enzyme during a second, subsequent duration.
72. (Cancelled).
73. (Previously presented) The system of claim 71, wherein the proteolytic enzyme comprises at least one enzyme selected from the group consisting of keratinase enzymes, proteinase K, trypsins, chymotrypsins, pepsins, chymosins, cathepsins, subtilisins, elastases, collagenases, endopeptidases, peptidases, oligopeptidase, thermolysins, bacillolysin, mycilysins, carboxypeptidases, leucyl aminopeptidases, aminopeptidases, extremthermophilic proteases, carbonyl hydrolase, papain, pancreatin, streptokinase, streptodornase, ficin, carboxypeptidase, chymopapain, and bromelin.
74. (Previously presented) The system of claim 71, wherein the proteolytic enzyme comprises *Bacillus licheniformis* PWD-1 keratinase.
75. (Withdrawn) The system of claim 71, wherein the proteolytic enzyme comprises a protease enzyme.
76. (Withdrawn) The system of claim 75, wherein the protease enzyme comprises a carbonyl hydrolase.

77. (Withdrawn) The system of claim 76, wherein the carbonyl hydrolase comprises subtilisin.
78. (Withdrawn) The system of claim 77, wherein the subtilisin comprises a mutant of wild-type *Bacillus amyloliquefaciens* subtilisin, comprising one or more amino acid substitutions, additions, or deletions.
79. (Withdrawn) The system of claim 75, wherein the protease enzyme comprises at least one enzyme selected from the group consisting of: papain, pancreatin, trypsin, chymotrypsin, pepsin, streptokinase, streptodornase, ficin, carboxypeptidase, aminopeptidase, chymopapain, bromelin, and subtilisin.
80. (Previously presented) A system comprising:
- (a) one or more articles susceptible to contamination by infectious prion protein;
  - (b) means for heating said articles;
  - (c) *Bacillus licheniformis* PWD-1 keratinase; and
  - (d) means for exposing the heated articles to the *Bacillus licheniformis* PWD-1 keratinase,
- wherein said articles are characterized by a first elevated temperature of at least 40°C and not more than about 150°C during a first duration, and wherein said articles are characterized by a second elevated temperature in a range of from about 50°C to about 65°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase during a second, subsequent duration.
81. (Cancelled).
82. (Previously presented) A system comprising:
- (a) one or more articles susceptible to contamination by infectious prion protein;

(b) means for heating said articles;

(c) *Bacillus licheniformis* PWD-1 keratinase; and

(d) means for exposing the articles to *Bacillus licheniformis* PWD-1 keratinase,

wherein said articles are characterized by an elevated temperature of from about 40°C to about 60°C and exposure to the *Bacillus licheniformis* PWD-1 keratinase.

83. (Cancelled).

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**Expires: August 10, 2005**



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